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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/614,947	07/12/2000	Russell A. Brierley	02655-046005	2510

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07/29/2002

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EXAMINER

SAUD, CHRISTINE J

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 07/29/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/614,947

Applicant(s)

BRIERLY et al.

Examiner

Christine Saoud

Art Unit

1647



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 7, 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-21 is/are allowed.
- 6) ☒ Claim(s) 22-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Claims 1 and 22-25 have been amended as requested in the amendment of paper #8, filed 07 May 2002. Claims 1-26 are pending in the instant application.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.
4. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn. The Terminal Disclaimer filed, paper #10, is proper and has been entered into the instant application.
5. Applicant's arguments with respect to claims 22-26 have been considered but are moot in view of the new ground(s) of rejection.

Specification

6. The attempt to incorporate subject matter into this application by reference to the previously filed applications by amendment in paper #8 is improper because it is not in

conformance with M.P.E.P. 608.04(b) because the amendment was not part of the original disclosure. Such amendment does not enjoy the status as part of the original disclosure in an application filed under 37 CFR 1.53 unless it is referred to in the oath or declaration filed therewith. Once an oath or declaration is submitted in an application filed under 37 CFR 1.53 identifying the papers which the inventor(s) has "reviewed and understands" as required by 37 CFR 1.63, the original disclosure of the application is defined and cannot be altered merely by filing of a subsequent oath or declaration referring to different papers. If the application is filed without an executed oath or declaration pursuant to 37 CFR 1.53(b), the original oath or declaration submitted later than the filing date must refer to the preliminary amendment filed along with the application in order to comply with 37 CFR 1.63.

The recitation "which is incorporated herein by reference in its entirety" should be deleted from the continuing data since it is new matter.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Chang et al. (U.S. Pat. No. 5,288,931), Hart et al. (Biotechnol. Appl. Biochem. 20: 217-232, 1994) and Holtz et al. (U.S. Pat. No. 5,231,178)

Chang et al. teach a method for refolding misfolded IGF-I, including an unfolding/refolding buffer with a pH between 7.5 and 10.5. Misfolded IGF-I has significantly reduced biological activity and therefore, correct biologically active conformation are essential for processing functional proteins (col. 1, lines 54-69 and col. 2, lines 1-2). Various buffers are suitable to obtain this pH range and include CAPSO, AMP, CAPS, CHES, TRIS, and sodium acetate (col. 10, lines 8-17). The buffer also contains "the minimum amount of chaotropic agent and reducing agent necessary substantially to solubilize the IGF-I and allow refolding" (col. 9, lines 52-60). Examples of suitable reducing agents are DTT, BME, and cysteine. The preferred reducing agent is DTT at about 2-4 μ M, BME at about 1-2 μ M, or cysteine at about 2-4 μ M (col. 10, lines 28-30). Applicants acknowledge in the instant Specification that borate is also a suitable buffering agent (as is TRIS). Hart et al. teach optimal conditions for IGF-I protein refolding including a refolding buffer with 2M urea, 1M NaCl, and 20% ethanol (see abstract). These references together teach the buffer conditions of the claims, but do not teach refolding of IGF-I produced in yeast.

Holtz et al. disclose a method of purification of IGF-I produced in transformed yeast. This IGF could be human and is necessarily recombinant. The promoter and transcription elements are specific for *P. pastoris* indicating a preference for this host (col. 5, lines 53-69 and col. 6, lines 1-9). Holtz et al. does not teach unfolding/refolding buffer and methods.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to practice the method of refolding of IGF-I as described by Chang et al. and Hart et al. with the recombinant yeast produced IGF-I of Holtz et al. because Chang et al. teach the importance of correctly folded IGF-I for biological activity. One of ordinary skill in the art would expect to obtain properly folded IGF-I because Chang et al. and Hart et al. teach that this is the result of the refolding method. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art because the production of correctly folded IGF-I is desired in order to obtain a molecule with full biological activity, recombinant production of IGF-I can result in misfolded IGF-I, the method of Holtz et al. provides a process for production of large quantities of IGF-I in yeast, and the teachings of Hart et al. and Chang et al. provide motivation and means for obtaining correctly folded IGF-I.

Conclusion

9. Claims 1-21 are allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Christine J. Saoud, Ph.D., whose telephone number is (703) 305-7519. The Examiner can normally be reached on Monday to Thursday from 8AM to 3PM. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. §§ 1.6(d) and 1.8). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

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Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternate number. Official papers filed After Final rejection filed by fax should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

**CHRISTINE J. SAOUD
PRIMARY EXAMINER**

Christine J. Saoud